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NEWS 37 May 15 MEDLINE file segment of TOXCENTER reloaded
NEWS 38 May 15 Supporter information for ENCOMPAT and ENCOMPLIT updated
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FULL ESTIMATED COST		

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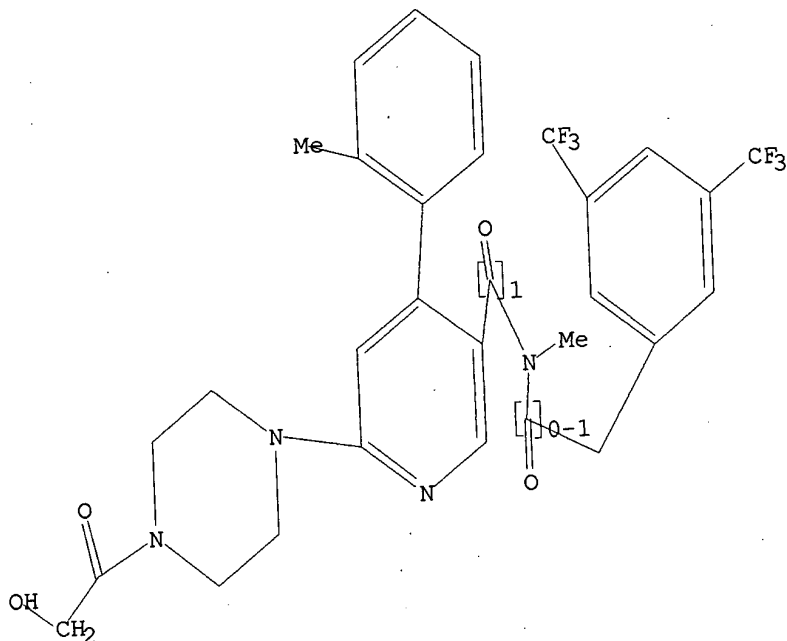
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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

L1 STR



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SAMPLE SEARCH INITIATED 08:31:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

0 ANSWERS

100.0% PROCESSED 1 ITERATIONS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1.

=> s l1 sss full

FULL SEARCH INITIATED 08:32:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6 TO ITERATE

1 ANSWERS

100.0% PROCESSED 6 ITERATIONS
SEARCH TIME: 00.00.01

L3 1 SEA SSS FUL L1

=> file caplus
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ENTRY	SESSION
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=> s 13
L4

3 L3

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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 2003:57902 CAPLUS
DN 138:117662
TI Use of NK-1 receptor antagonists for the treatment of brain, spinal or nerve injury
IN Hoffmann, Torsten; Nimmo, Alan John; Sleight, Andrew; Vankan, Pierre; Vink, Robert
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006016	A2	20030123	WO 2002-EP7323	20020703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

US 2003083345 A1 20030501

EP 2001-116812 A 20010710
 US 2002-187587 20020702
 EP 2001-116812 A 20010710

OS MARPAT 138:117662

IT 401891-32-5

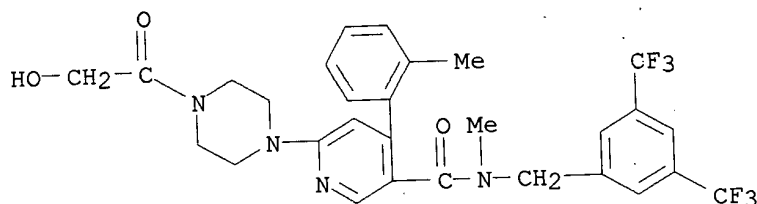
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(NK-1 receptor antagonist for treatment of brain, spinal or nerve injury)

RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



AB The invention discloses the use of an NK-1 receptor antagonist (Markush included), e.g. N-(3,5-bis-trifluoromethylbenzyl)-N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolynicotinamide, optionally in combination with a magnesium salt, for the treatment and/or prevention of brain, spinal or nerve injury. The invention also relates to pharmaceutical comps. comprising one or more such NK-1 receptor antagonists, optionally in combination with a magnesium salt, and a pharmaceutically acceptable excipient, for the treatment and/or prevention of brain, spinal or nerve injury.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

AN 2002:832668 CAPLUS

DN 137:337901

TI Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia

IN Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; Sleight, Andrew John; Vankan, Pierre

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO. DATE

PI WO 2002085458 A2 20021031 WO 2002-EP1085 20020202
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 EP 2001-109853 A 20010423
 US 2003004157 A1 20030102 US 2002-71570 20020208
 EP 2001-109853 A 20010423

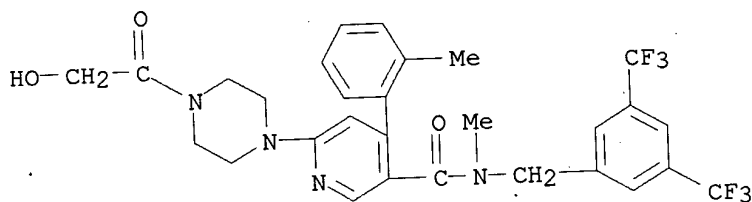
OS MARPAT 137:337901

IT 401891-32-5

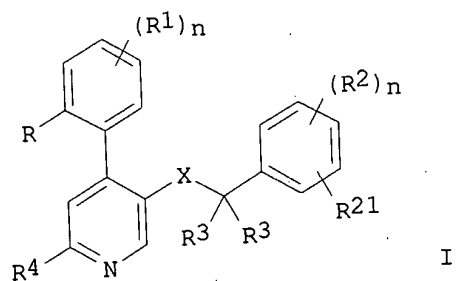
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (prepn. and use of amides as NK-1 receptor antagonists against benign
 prostatic hyperplasia)

RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-
 (hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA
 INDEX NAME)



GI



AB Use of an NK-1 receptor antagonist for the treatment or prevention of
 benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1
 receptor antagonists are compds. of the general formula [I; R = H, alkyl,
 alkoxy, halo, CF₃; R₁ = H, halo; RR₁ = CH:CHCH:CH; R₂, R₂₁ = H, halo,
 CF₃, alkyl, alkoxy, cyano; R₂R₂₁ = CH:CHCH:CH, optionally substituted by
 1-2 alkyl, halo, alkoxy; R₃ = H, alkyl; R₃R₃C = cycloalkyl; R₄ = H,

<5/24/2003>

Patel

N(R5)2, NR5(CH2)nOH, cyclic tertiary amine, etc.; X = CONR5, (CH2)pO, NR5(CH2)p, etc.; R5 = H, cycloalkyl, Ph, PhCH2, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1.1lambda.6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.1lambda.6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (prepn. given) oxone were stirred 2 days at room temp. to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.1lambda.6-thiomorpholin-4-yl)-4-o-tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate wt. by 58% after 39 wk.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 2002:157739 CAPLUS

DN 136:216651

TI Preparation of 4-phenylpyridines as neurokinin-1 receptor antagonists
IN Godel, Thierry; Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz

PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 108 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002016324	A1	20020228	WO 2001-EP8686	20010727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002012118	A5	20020304	EP 2000-117003 A	20000808
			AU 2002-12118	20010727
			EP 2000-117003 A	20000808
			WO 2001-EP8686 W	20010727
EP 1309559	A1	20030514	EP 2001-980219	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			EP 2000-117003 A	20000808
			WO 2001-EP8686 W	20010727
US 2002040040	A1	20020404	US 2001-922066	20010803
			EP 2000-117003 A	20000808
NO 2003000632	A	20030207	NO 2003-632	20030207
			EP 2000-117003 A	20000808
			WO 2001-EP8686 W	20010727

OS MARPAT 136:216651

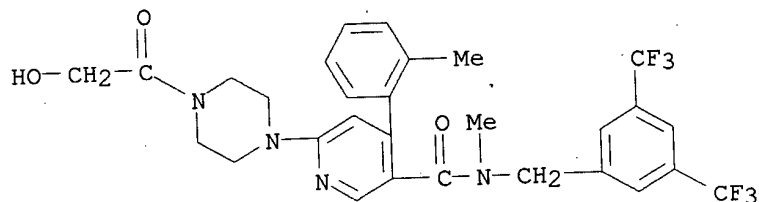
IT 401891-32-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

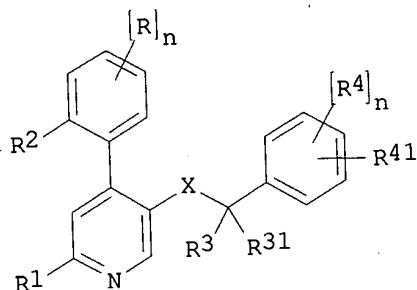
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



GI



I

AB The title compds. [I; R = H, halo; R1 = (C.tplbond.C)mR11, (CR'=CR'')mR11 (wherein R11 = halo, CN, aryl, etc.; R', R'' = H, OH, alkyl, etc.); R2 = H, alkyl, alkoxy, halo, CF3; R3, R31 = H, alkyl or form together with the C atom to which they are attached a cycloalkyl group; R4, R41 = H, halo, CF3, alkyl, alkoxy; R and R2 or R4 and R41 may be together CH=CHCH=CH, optionally substituted by one or two substituents selected from alkyl, halo or alkoxy; X = CONR8, (CH2)pO, (CH2)pNR8, NR8CO, NR8(CH2)p (wherein R8 = H, alkyl); n = 1-2; m = 0-4; p = 1-2] which are antagonists of the Neurokinin 1 (NK-1, substance P) receptor, and therefore useful in the treatment of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R = H; R1 = N(OH)CH2CH2OH; R2 = Me; R3, R31 = Me; R4 = 3-CF3; R41 = 5-CF3; X = NMeCO] which showed pKi of 9.29 in human NK1 receptor assay, was given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
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SEARCH CHARGES
DISPLAY CHARGES

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CAPLUS FEE (5%)

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

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ENTRY	SESSION
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NEWS 40 May 19 Simultaneous left and right truncation added to WSCA
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation

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SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

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DICTIONARY FILE UPDATES: 22 MAY 2003 HIGHEST RN 519137-84-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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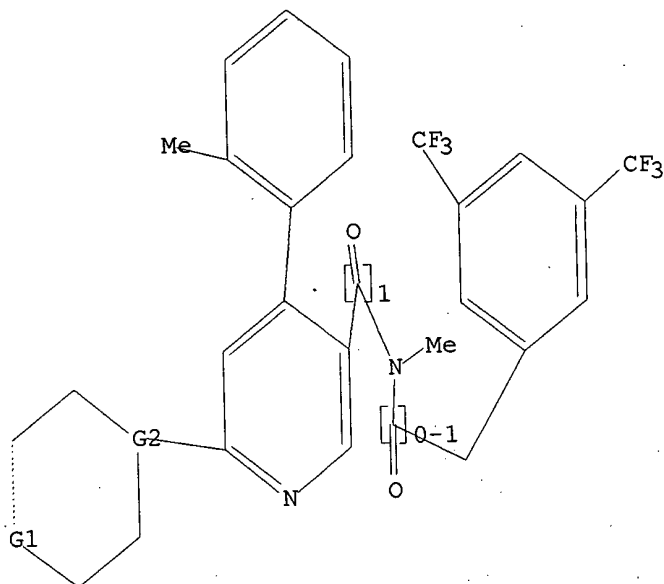
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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

L1 STR



G1 C,O,N

G2 C,N

Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED 8 ITERATIONS
SEARCH TIME: 00.00.01

6 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8 TO 329
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

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FULL SEARCH INITIATED 08:43:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 63 TO ITERATE

100.0% PROCESSED 63 ITERATIONS
SEARCH TIME: 00.00.01

39 ANSWERS

L3 39 SEA SSS FUL L1

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 08:43:57 ON 24 MAY 2003
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FILE COVERS 1907 - 24 May 2003 VOL 138 ISS 22
FILE LAST UPDATED: 23 May 2003 (20030523/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4

7 L3

=> s 14 fbib hitstr abs total
MISSING OPERATOR L4 FBIB

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> d 14 fbib hitstr abs total

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2003:57902 CAPLUS

DN 138:117662

TI Use of NK-1 receptor antagonists for the treatment of brain, spinal or nerve injury

IN Hoffmann, Torsten; Nimmo, Alan John; Sleight, Andrew; Vankan, Pierre; Vink, Robert

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006016	A2	20030123	WO 2002-EP7323	20020703
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

US 2003083345

A1

20030501

EP 2001-116812 A 20010710

US 2002-187587 20020702

EP 2001-116812 A 20010710

OS MARPAT 138:117662

IT 290296-84-3 290296-85-4 290296-86-5

290296-89-8 290296-93-4 290296-94-5

290296-95-6 290296-96-7 290296-98-9

290296-99-0 290297-00-6 290297-57-3

391674-85-4 391674-86-5 391674-90-1

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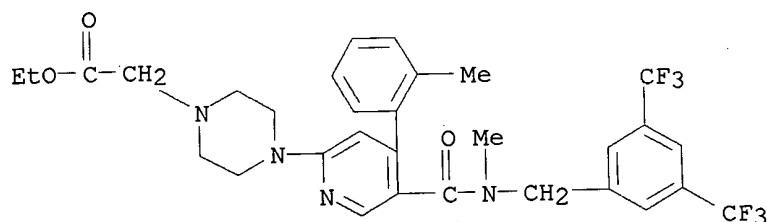
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

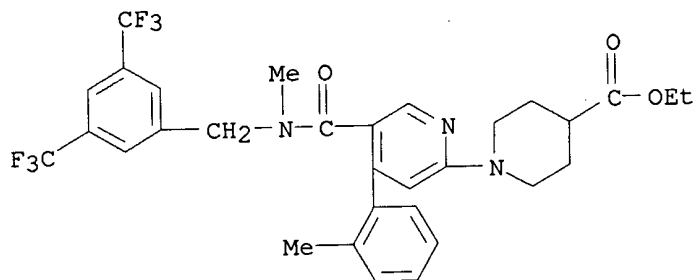
(NK-1 receptor antagonist for treatment of brain, spinal or nerve injury)

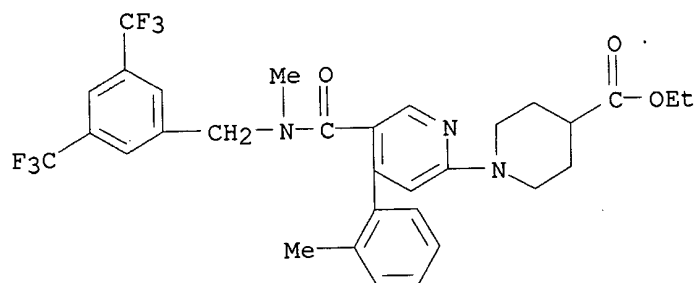
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CN 1-Piperazineacetic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI)
 (CA INDEX NAME)

RN 290296-85-4 CAPLUS

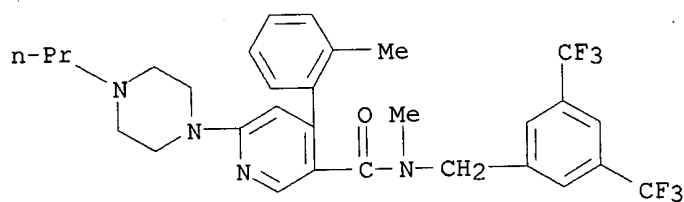
CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)





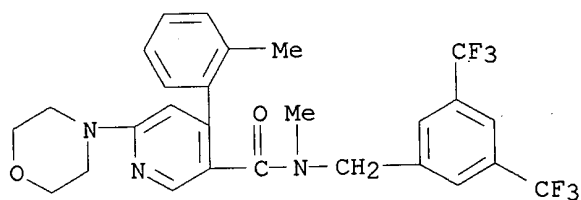
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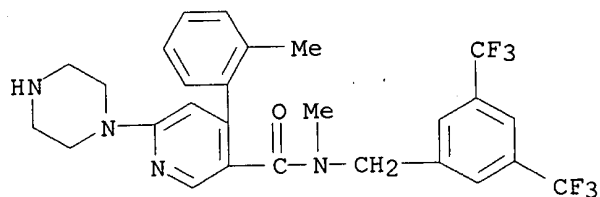
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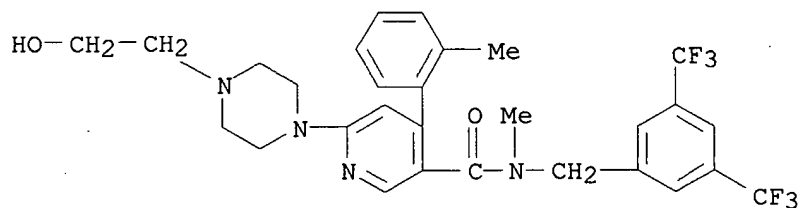
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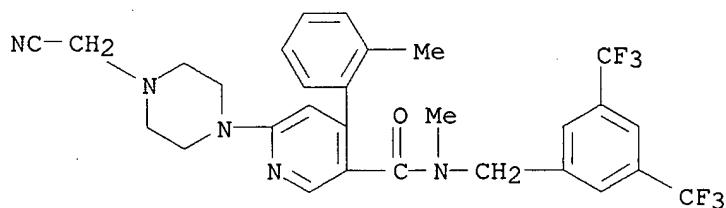
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

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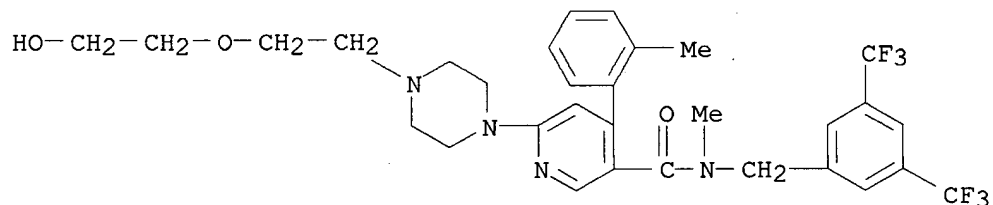
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CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethoxy)ethyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



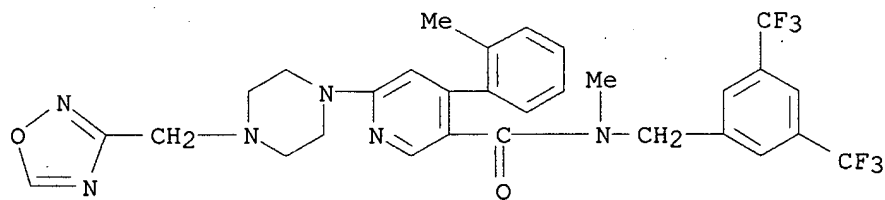
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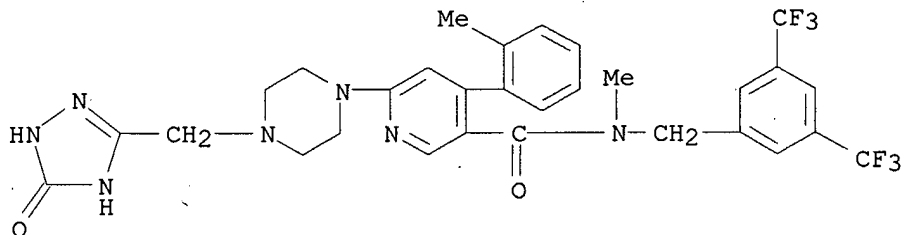
RN 290296-98-9 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-[4-(1,2,4-oxadiazol-3-ylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



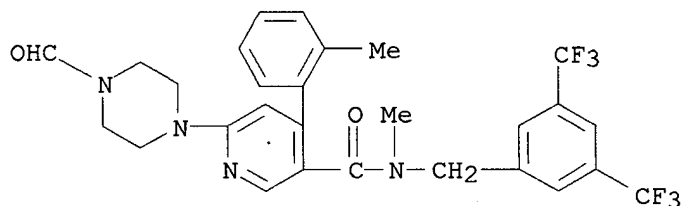
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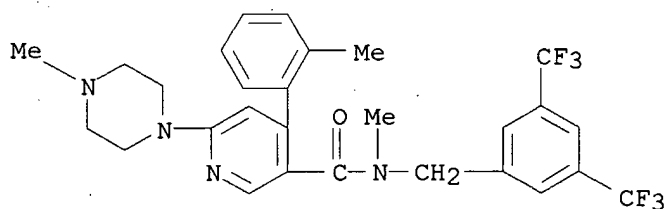
RN 290297-00-6 CAPLUS

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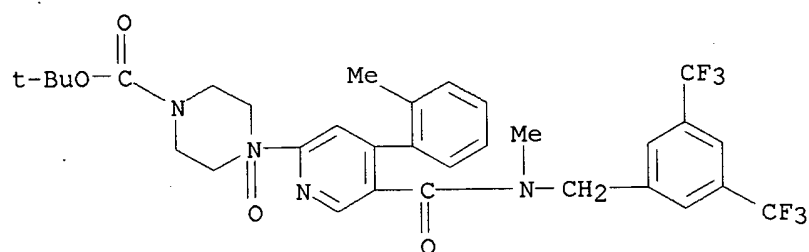
RN 290297-57-3 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-
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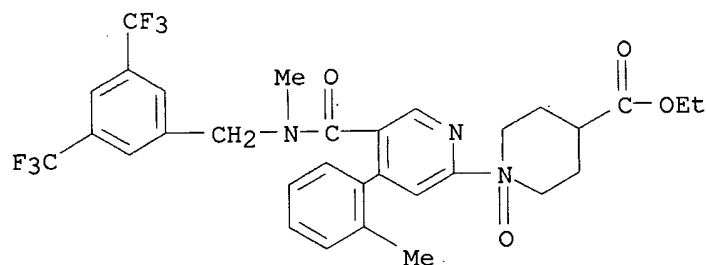
RN 391674-85-4 CAPLUS

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methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-,
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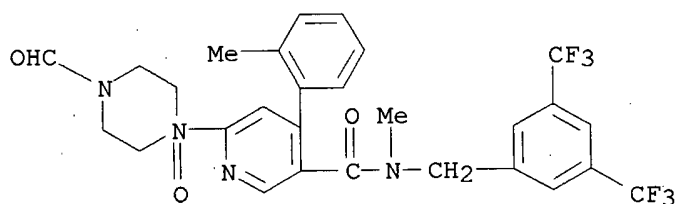
RN 391674-86-5 CAPLUS

RN 3916/4-86-5 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester, 1-oxide (9CI) (CA INDEX NAME)



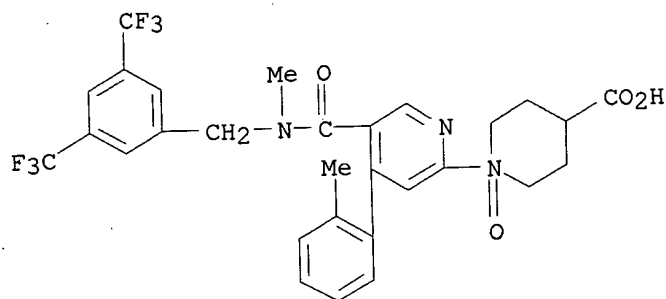
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RN 391674-90-1 CAPLUS
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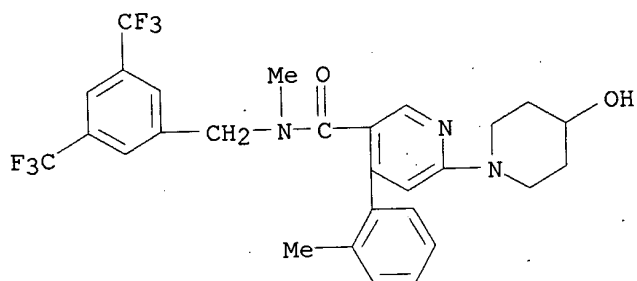


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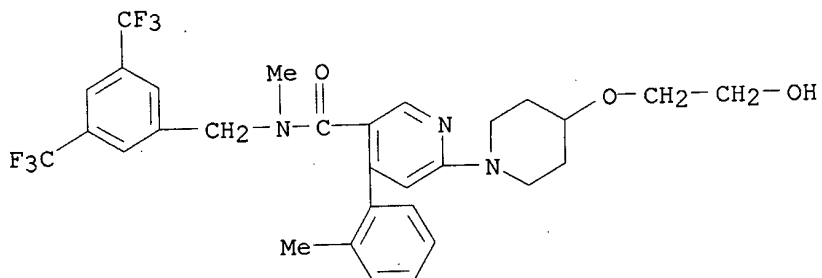
RN. 391675-01-7 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1-oxide (9CI)
(CA INDEX NAME)



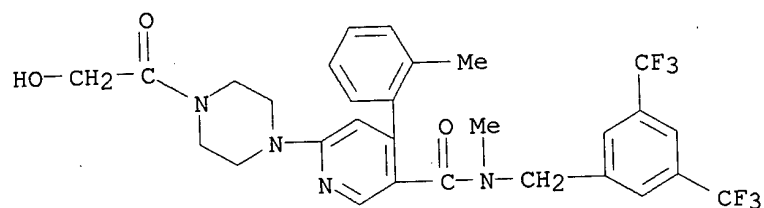
RN 393508-72-0 CAPLUS
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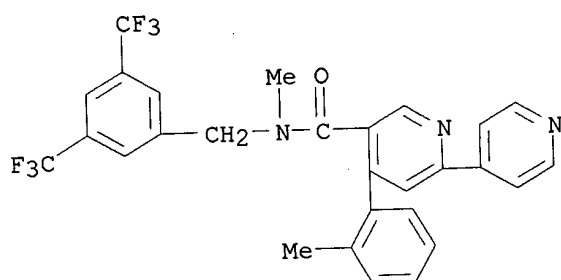
RN 393508-73-1 CAPLUS
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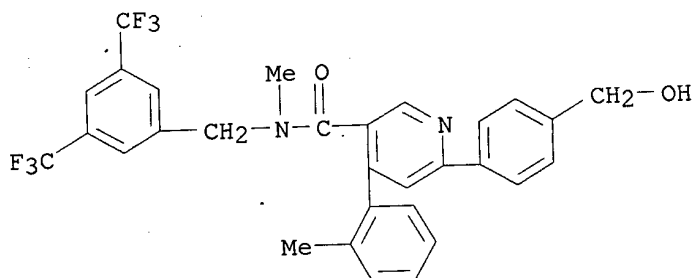
RN 401891-32-5 CAPLUS
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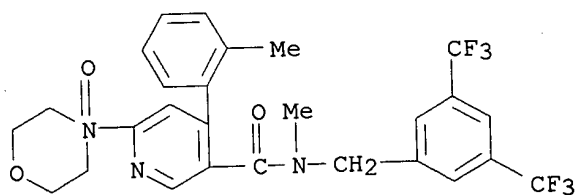
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 CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



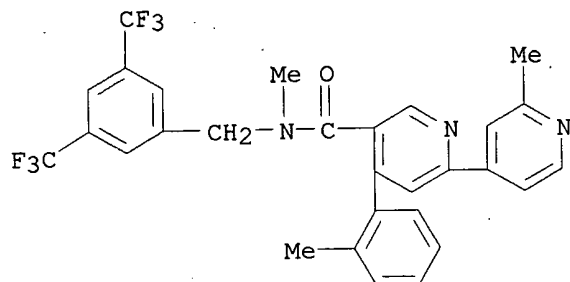
RN 401891-70-1 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxymethyl)phenyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401892-63-5 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 474026-12-5 CAPLUS
 CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N,2'-dimethyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



AB The invention discloses the use of an NK-1 receptor antagonist (Markush included), e.g. N-(3,5-bis-trifluoromethylbenzyl)-N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide, optionally in combination with a magnesium salt, for the treatment and/or prevention of brain, spinal or nerve injury. The invention also relates to pharmaceutical compns. comprising one or more such NK-1 receptor antagonists, optionally in combination with a magnesium salt, and a pharmaceutically acceptable excipient, for the treatment and/or prevention of brain, spinal or nerve injury.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2002:832668 CAPLUS

DN 137:337901

TI Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia

IN Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; Sleight, Andrew John; Vankan, Pierre

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085458	A2	20021031	WO 2002-EP1085	20020202
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004157	A1	20030102	EP 2001-109853 A	20010423
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OS MARPAT 137:337901

IT 290296-86-5 290296-89-8 290296-93-4

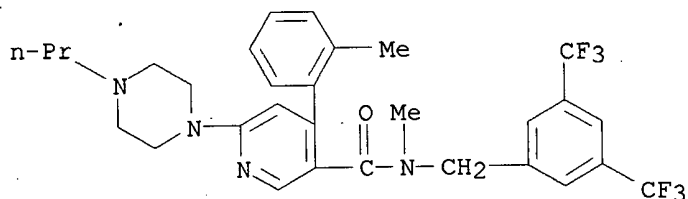
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 401891-70-1 401892-63-5 474026-12-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(prepn. and use of amides as NK-1 receptor antagonists against benign
 prostatic hyperplasia)

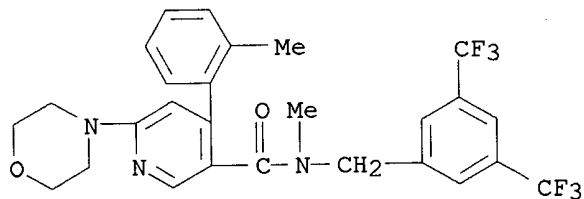
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CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-
 4-(2-methylphenyl)-6-(4-propyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



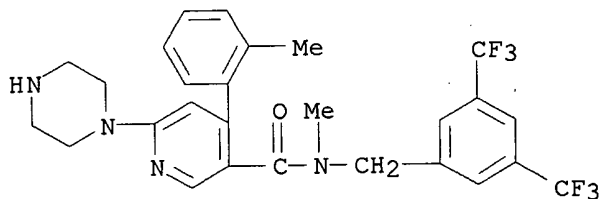
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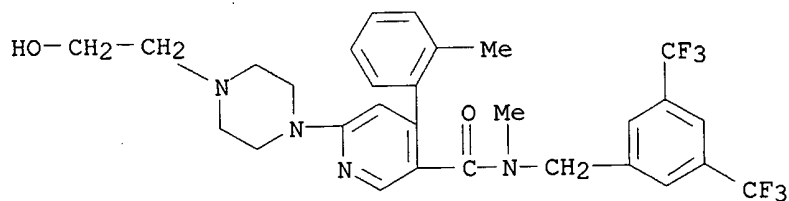
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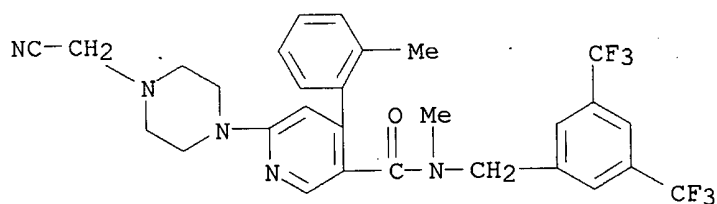
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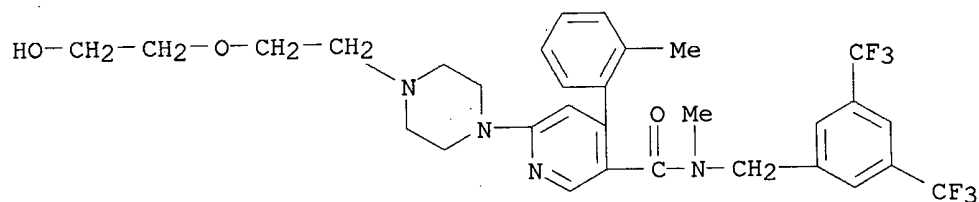
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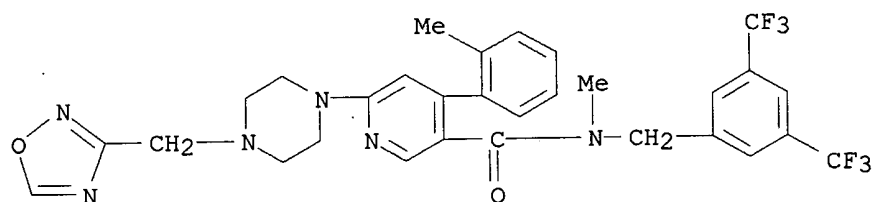
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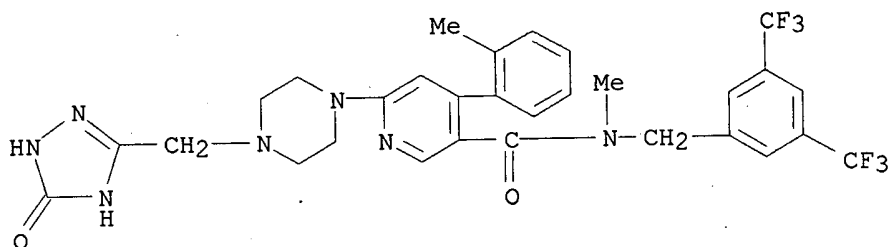
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RN 290296-99-0 CAPLUS

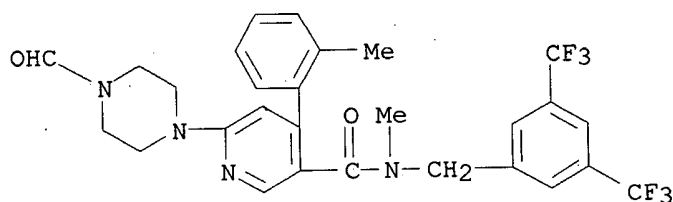
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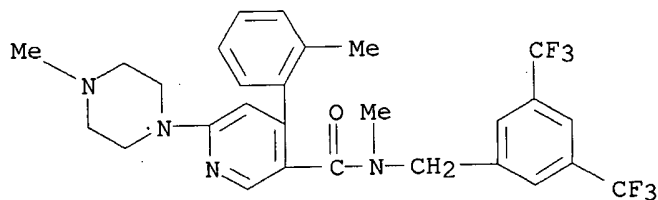
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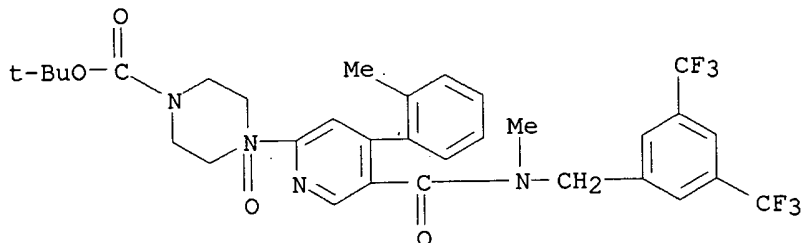
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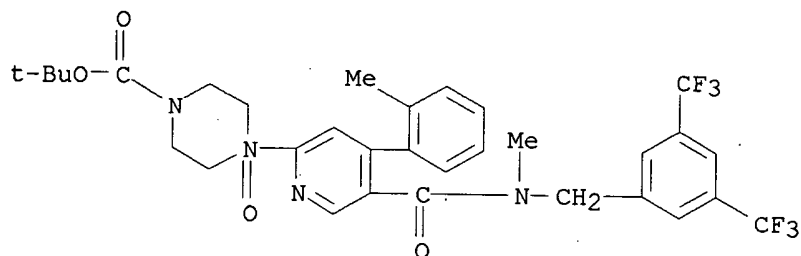
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RN 391674-85-4 CAPLUS

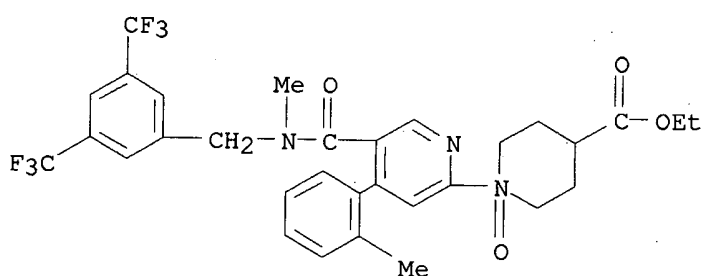
CN 1-Piperazinecarboxylic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester, 4-oxide (9CI) (CA INDEX NAME)





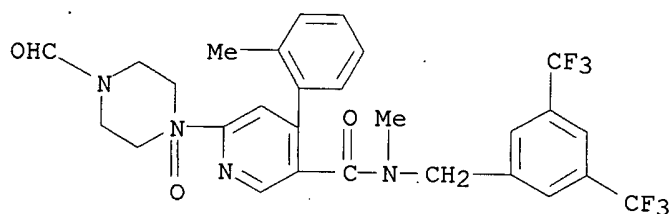
RN 391674-86-5 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester, 1-oxide (9CI) (CA INDEX NAME)



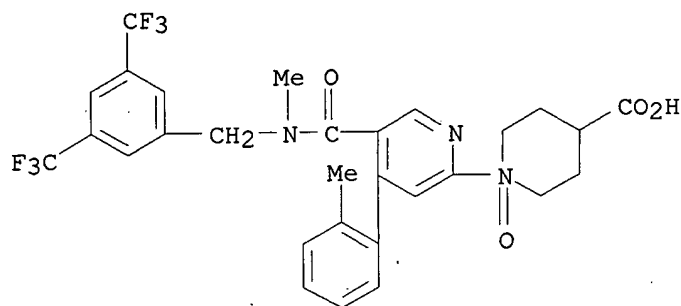
RN 391674-90-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-oxido-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



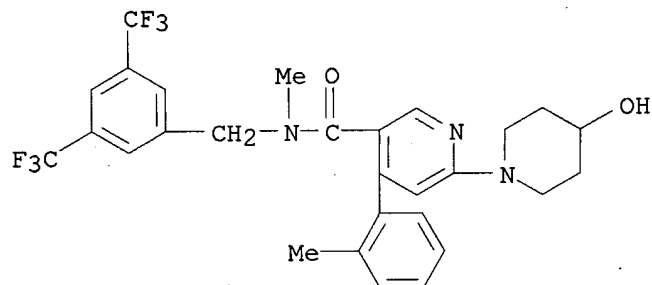
RN 391675-01-7 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1-oxide (9CI) (CA INDEX NAME)



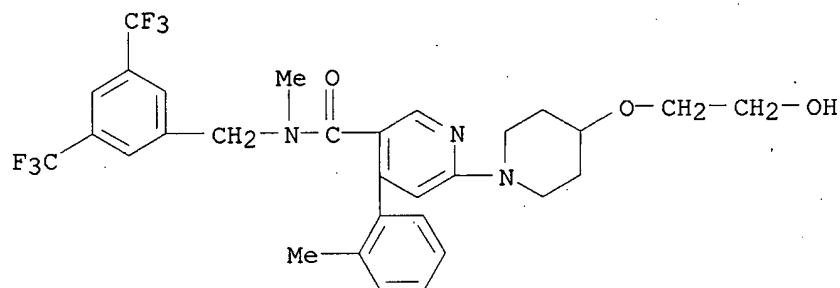
RN 393508-72-0 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-hydroxy-1-piperidinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



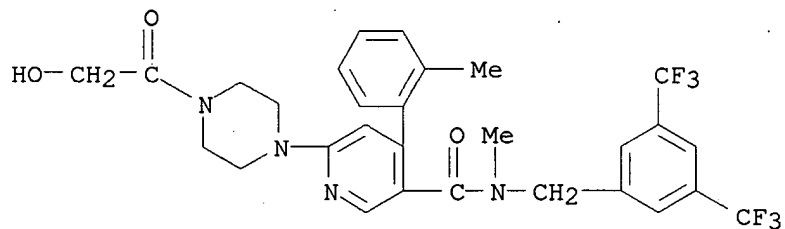
RN 393508-73-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethoxy)-1-piperidinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



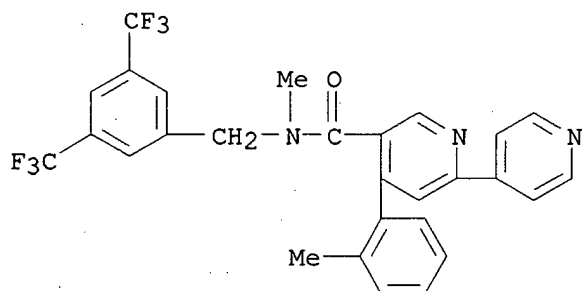
RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



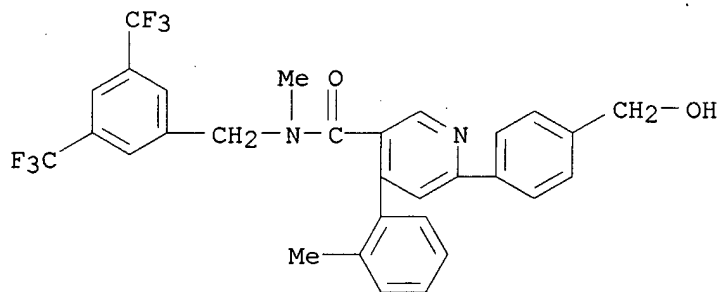
RN 401891-35-8 CAPLUS

CN [2,4'-Bipyridine]-5-carboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



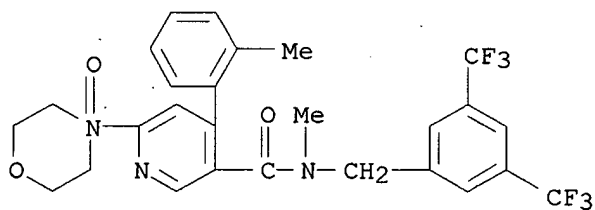
RN 401891-70-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxymethyl)phenyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



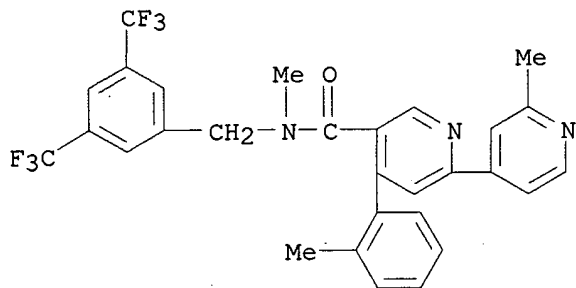
RN 401892-63-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)- (9CI) (CA INDEX NAME)

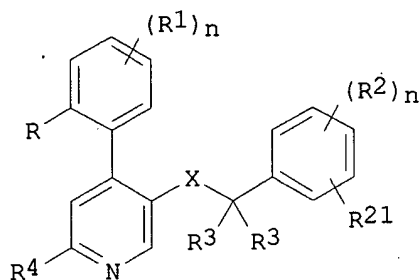


RN 474026-12-5 CAPLUS

CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N,2'-dimethyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



GI



I

AB Use of an NK-1 receptor antagonist for the treatment or prevention of benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1 receptor antagonists are compds. of the general formula [I; R = H, alkyl, alkoxy, halo, CF₃; R₁ = H, halo; RR₁ = CH:CHCH:CH; R₂, R₂₁ = H, halo, CF₃, alkyl, alkoxy, cyano; R₂R₂₁ = CH:CHCH:CH, optionally substituted by 1-2 alkyl, halo, alkoxy; R₃ = H, alkyl; R₃R₃C = cycloalkyl; R₄ = H, N(R₅)₂, NR₅(CH₂)_nOH, cyclic tertiary amine, etc.; X = CONR₅, (CH₂)_pO, NR₅(CH₂)_p, etc.; R₅ = H, cycloalkyl, Ph, PhCH₂, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1.λ.6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.λ.6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (prepn. given) oxone were stirred 2 days at room temp. to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.λ.6-thiomorpholin-4-yl)-4-o-tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate wt. by 58% after 39 wk.

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2002:157739 CAPLUS

DN 136:216651

TI Preparation of 4-phenylpyridines as neurokinin-1 receptor antagonists

IN Godel, Thierry; Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 108 pp..

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002016324	A1	20020228	WO 2001-EP8686	20010727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002012118	A5	20020304	EP 2000-117003 A	20000808
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			WO 2001-EP8686 W	20010727
EP 1309559	A1	20030514	EP 2001-980219	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			EP 2000-117003 A	20000808
			WO 2001-EP8686 W	20010727
US 2002040040	A1	20020404	US 2001-922066	20010803
			EP 2000-117003 A	20000808
NO 2003000632	A	20030207	NO 2003-632	20030207
			EP 2000-117003 A	20000808
			WO 2001-EP8686 W	20010727

OS MARPAT 136:216651

IT 401891-47-2P 401891-48-3P 401891-49-4P

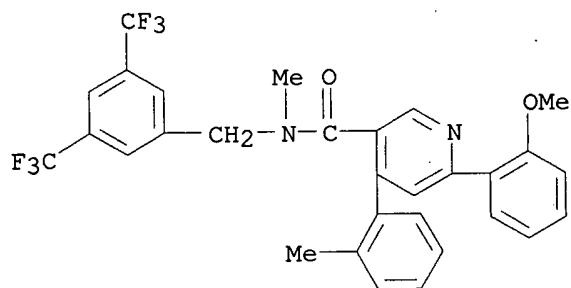
401891-69-8P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

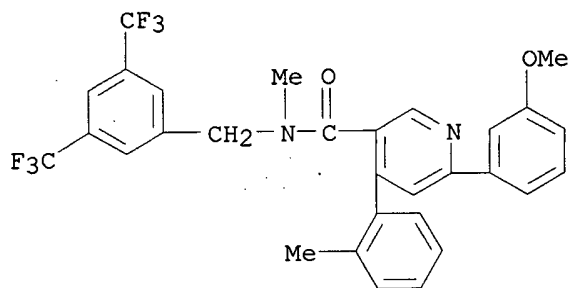
RN 401891-47-2 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(2-methoxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



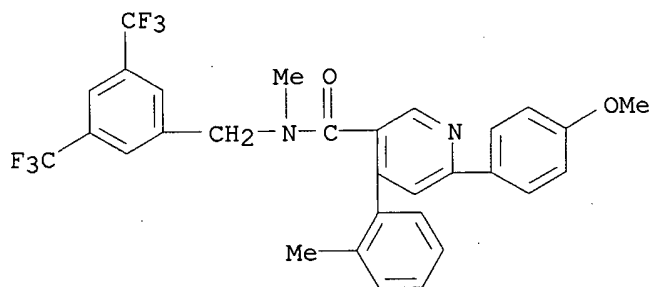
RN 401891-48-3 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(3-methoxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



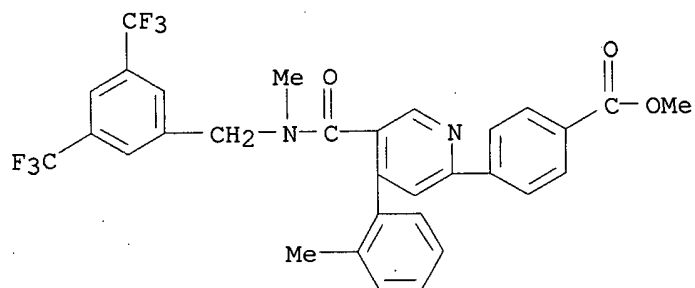
RN 401891-49-4 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-methoxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401891-69-8 CAPLUS

CN Benzoic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, methyl ester (9CI) (CA INDEX NAME)



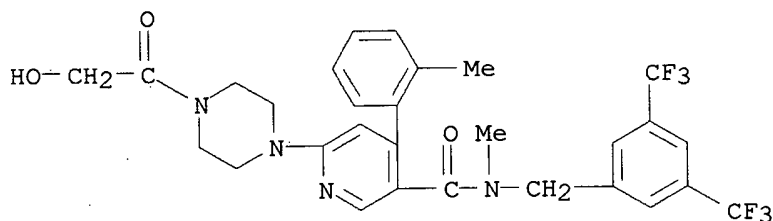
IT 401891-32-5P 401891-35-8P 401891-50-7P
401891-51-8P 401891-52-9P 401891-70-1P
401891-71-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

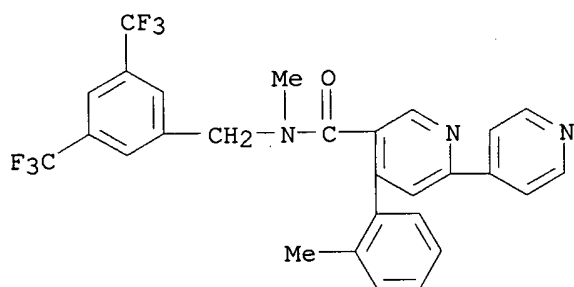
RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



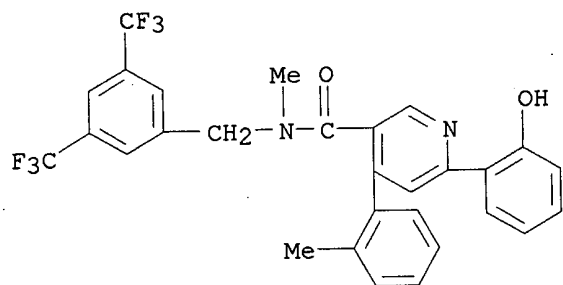
RN 401891-35-8 CAPLUS

CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



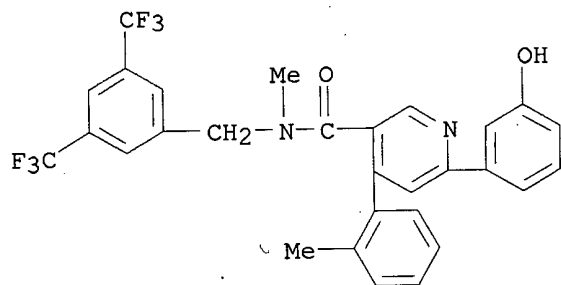
RN 401891-50-7 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(2-hydroxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



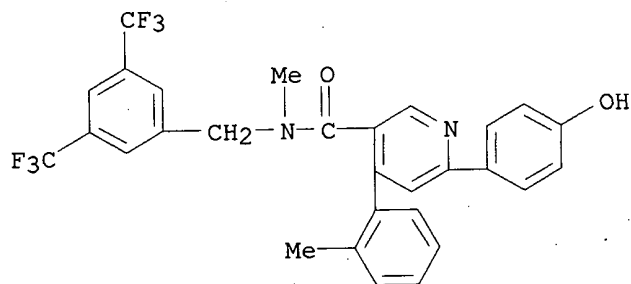
RN 401891-51-8 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(3-hydroxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



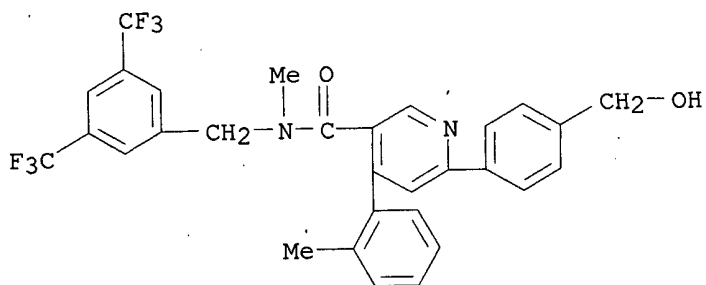
RN 401891-52-9 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-hydroxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

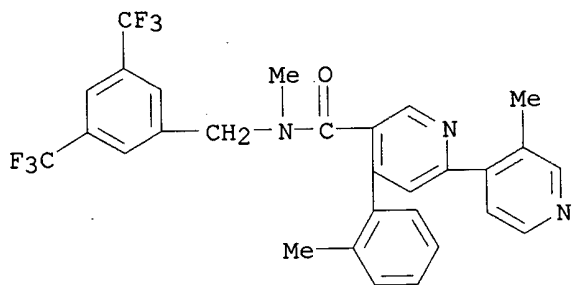


RN 401891-70-1 CAPLUS

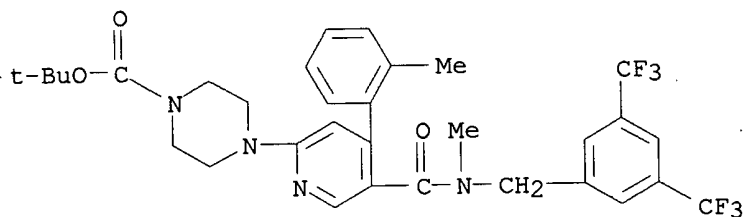
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxymethyl)phenyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



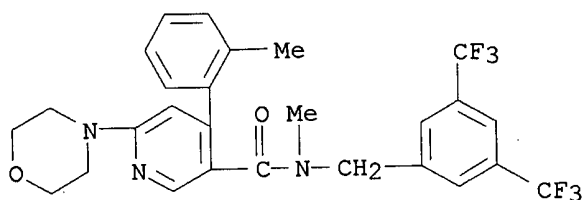
RN 401891-71-2 CAPLUS
 CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N,3'-dimethyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



IT 290296-83-2P 290296-89-8P 290296-93-4P
 401892-45-3P 401892-63-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)
 RN 290296-83-2 CAPLUS
 CN 1-Piperazinecarboxylic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

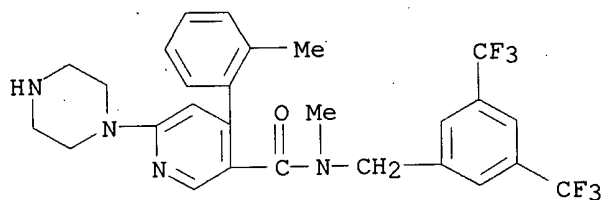


RN 290296-89-8 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



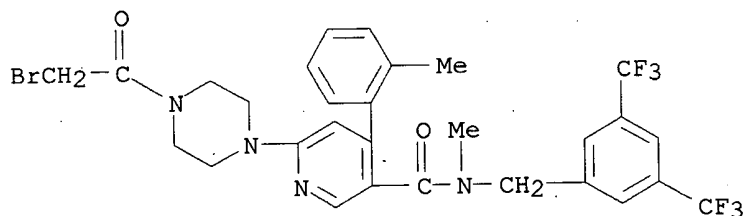
RN 290296-93-4 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



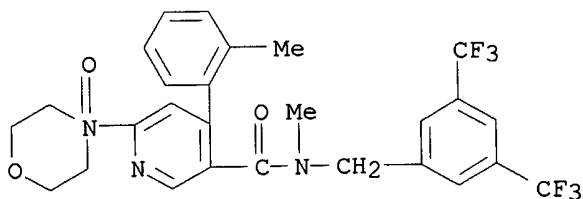
RN 401892-45-3 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(bromoacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

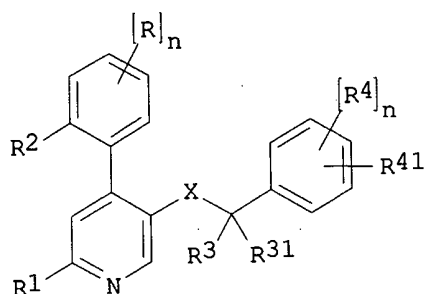


RN 401892-63-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)- (9CI) (CA INDEX NAME)



GI



I

AB The title compds. [I; R = H, halo; R1 = (C.tplbond.C)mR11, (CR'=CR'')mR11 (wherein R11 = halo, CN, aryl, etc.; R', R'' = H, OH, alkyl, etc.); R2 = H, alkyl, alkoxy, halo, CF3; R3, R31 = H, alkyl or form together with the C atom to which they are attached a cycloalkyl group; R4, R41 = H, halo, CF3, alkyl, alkoxy; R and R2 or R4 and R41 may be together CH=CHCH=CH, optionally substituted by one or two substituents selected from alkyl, halo or alkoxy; X = CONR8, (CH2)pO, (CH2)pNR8, NR8CO, NR8(CH2)p (wherein R8 = H, alkyl); n = 1-2; m = 0-4; p = 1-2] which are antagonists of the Neurokinin 1 (NK-1, substance P) receptor, and therefore useful in the treatment of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R = H; R1 = N(OH)CH2CH2OH; R2 = Me; R3, R31 = Me; R4 = 3-CF3; R41 = 5-CF3; X = NMeCO] which showed pKi of 9.29 in human NK1 receptor assay, was given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2002:90050 CAPLUS

DN 136:134681

TI Preparation of 4-phenylpyridine derivatives as neurokinin-1 receptor antagonists

IN Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008232	A1	20020131	WO 2001-EP8432	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002038030	A1	20020328	US 2001-901311	20010709
EP 1305319	A1	20030502	EP 2000-115846 A	20000724
			EP 2000-115846 A	20000724
			EP 2001-960529	20010720

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NO 2003000353

A

20030123

EP 2000-115846 A 20000724

WO 2001-EP8432 W 20010720

NO 2003-353 20030123

EP 2000-115846 A 20000724

WO 2001-EP8432 W 20010720

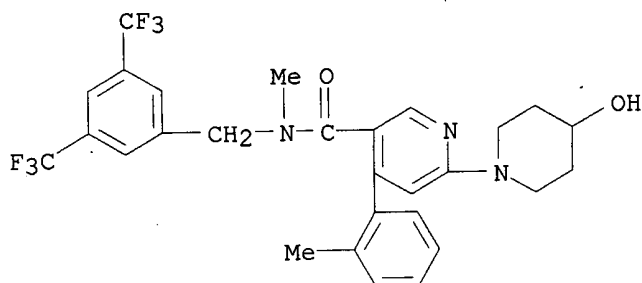
OS MARPAT 136:134681

IT **393508-72-0P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 393508-72-0 CAPLUS

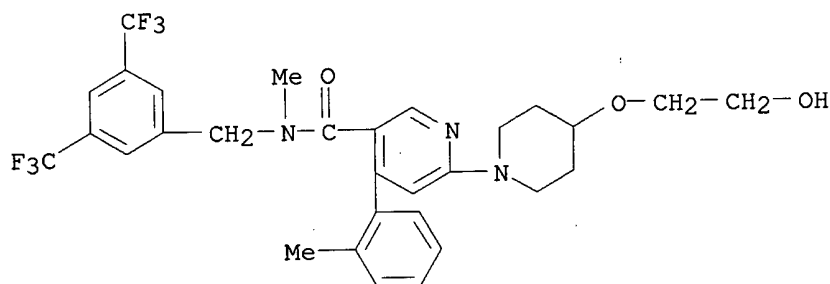
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-hydroxy-1-piperidiny)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

IT **393508-73-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

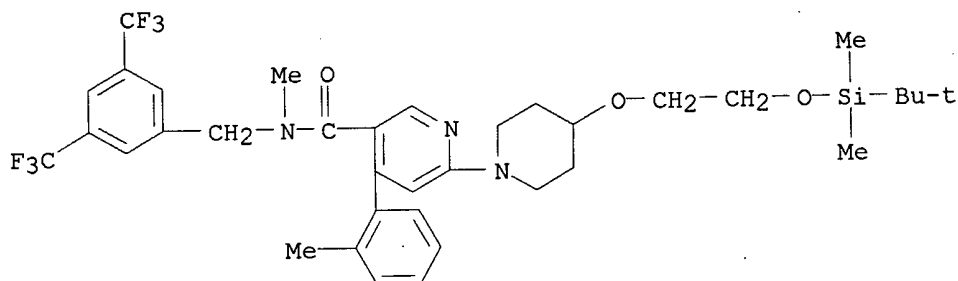
RN 393508-73-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethoxy)-1-piperidiny]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

IT **393508-85-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 393508-85-5 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[2-
 [[(1,1-dimethylethyl)dimethylsilyl]oxy]ethoxy]-1-piperidinyl]-N-methyl-4-
 (2-methylphenyl)- (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I or II; R1 = III, 2,3-dihydro-[1,4]oxazin-4-yl, imidazol-1-yl, [1,2,4]triazol-1-yl, NH(CH2)2OH, NR3COCH3, NR3COcyclopropyl; R2 = Me, Cl; R3 = H, Me; R = H, (CH2)2OH; n = 1-2] which have a good affinity of the NK-1 receptor and therefore they may be used in the treatment or prevention of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R1 = [1,2,4]triazol-1-yl; R2 = Me] which showed pKi of 8.4 against binding at human NK1 receptors in CHO cells, was given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7. CAPLUS COPYRIGHT 2003 ACS
 AN 2002:72051 CAPLUS
 DN 136:118387
 TI Preparation of N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivatives
 IN Hoffmann, Torsten; Poli, Sonia Maria; Schnider, Patrick; Sleight, Andrew
 PA F. Hoffmann-La Roche A.-G., Switz.
 SO PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006236	A1	20020124	WO 2001-EP7850	20010709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1303490 A1 20030423 EP 2000-115287 A 20000714
 EP 2001-949475 20010709
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2002045642 A1 20020418 EP 2000-115287 A 20000714
 WO 2001-EP7850 W 20010709
 US 2001-904059 20010712
 EP 2000-115287 A 20000714

NO 2003000154 A 20030113 NO 2003-154 20030113
 EP 2000-115287 A 20000714
 WO 2001-EP7850 W 20010709

OS MARPAT 136:118387

IT 290296-83-2P 290296-85-4P 290296-89-8P

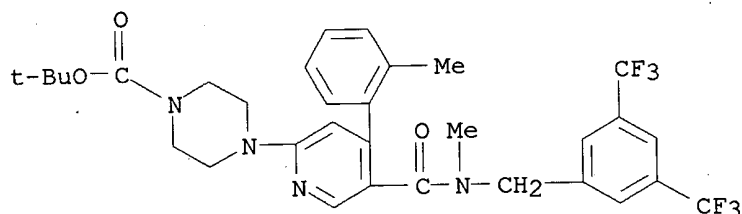
290297-00-6P 290297-11-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate product in prepn. of aminopyridine N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivs.)

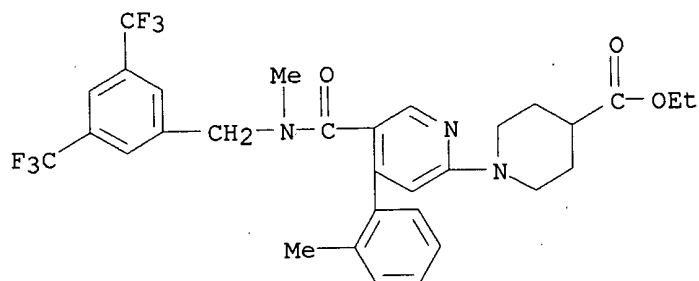
RN 290296-83-2 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 290296-85-4 CAPLUS

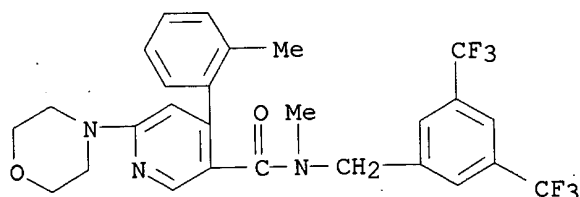
CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290296-89-8 CAPLUS

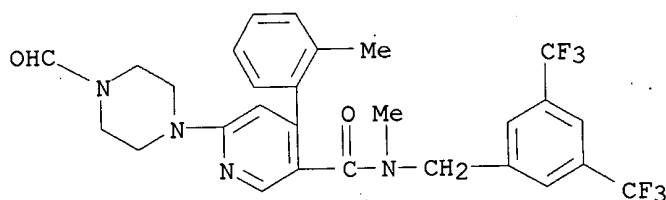
CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-

4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



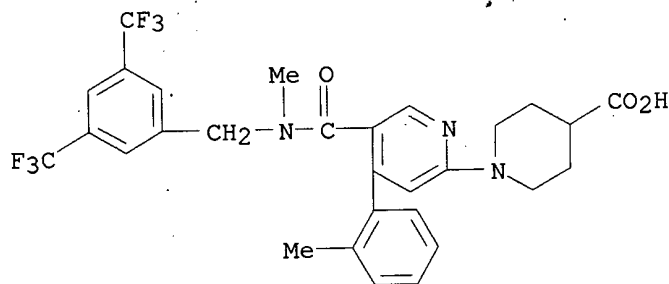
RN 290297-00-6 CAPLUS

CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 290297-11-9 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



IT 391674-85-4P 391674-86-5P 391674-88-7P

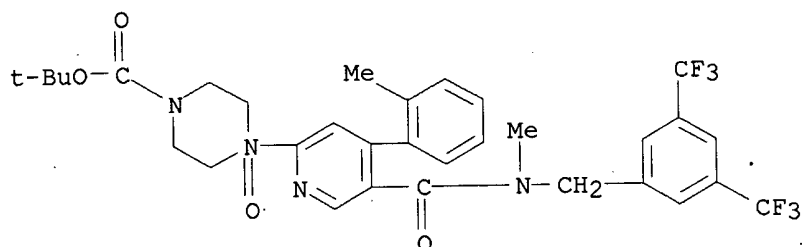
391674-90-1P 391675-01-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

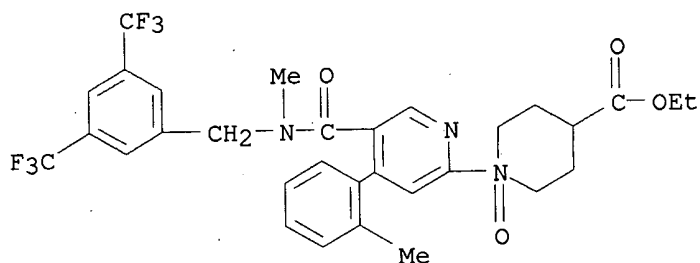
(prepn. of aminopyridine N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivs.)

RN 391674-85-4 CAPLUS

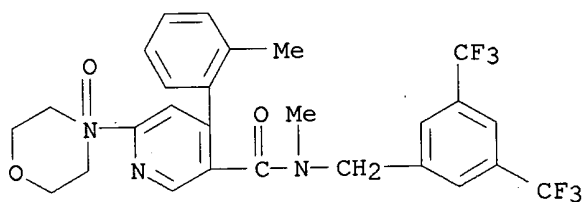
CN 1-Piperazinecarboxylic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester, 4-oxide (9CI) (CA INDEX NAME)



RN 391674-86-5 CAPLUS
 CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl-1]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl-, ethyl ester, 1-oxide (9CI) (CA INDEX NAME)

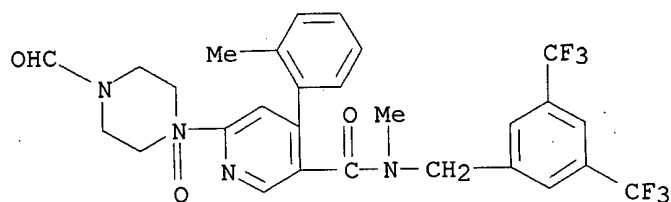


RN 391674-88-7 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)-, monohydrate (9CI) (CA INDEX NAME)

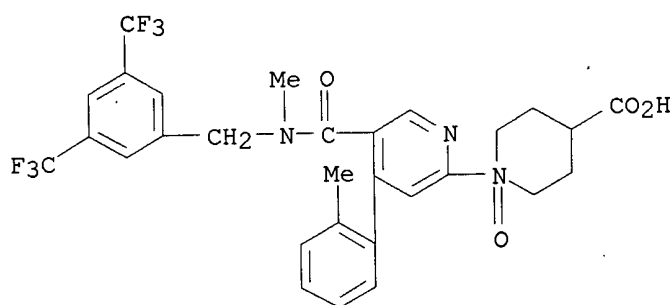


● H₂O

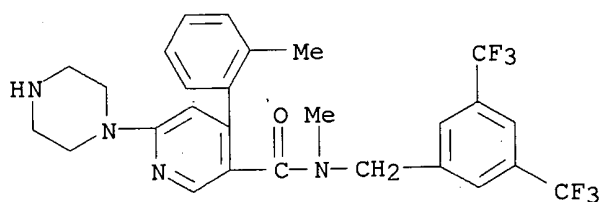
RN 391674-90-1 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-oxido-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



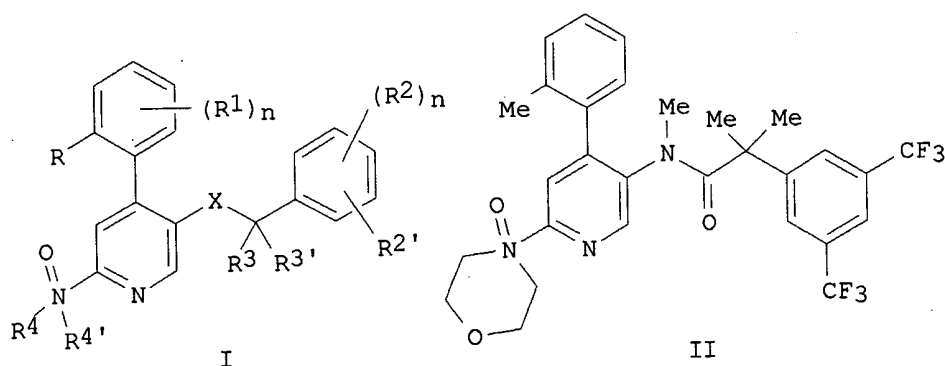
RN 391675-01-7 CAPLUS
 CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1-oxide (9CI)
 (CA INDEX NAME)



IT **290296-93-4**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant for prepn. of aminopyridine N-oxides as NK1 receptor
 antagonist prodrugs of 4-phenylpyridine derivs.)
 RN 290296-93-4 CAPLUS
 CN 3-Pyridinecarboxamide, N-[[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



GI



AB The prepn. is described for N-oxides (I) wherein R is hydrogen, lower alkyl, lower alkoxy, or trifluoromethyl; R1 is hydrogen or halogen; or R and R1 may be together with the ring carbon atoms to which they are attached $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$; R2 and R2' are independently from each other hydrogen, halogen, trifluoromethyl, lower alkoxy or cyano; or R2 and R2' may be together $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$, optionally substituted by one or two substituents selected from lower alkyl or lower alkoxy; R3, R3' are independently from each other hydrogen, lower alkyl or cycloalkyl; R4, R4' are independently from each other $-(\text{CH}_2)_m\text{OR}_6$ or lower alkyl; or R4 and R4' form together with the N-atom to which they are attached a cyclic tertiary amine with substituent R5 chosen from hydrogen, hydroxy, lower alkyl, lower alkoxy, $-(\text{CH}_2)_m\text{OH}$, $-\text{COOR}_3$, $-\text{CON}(\text{R}_3)_2$, $-\text{N}(\text{R}_3)\text{CO}$ -lower alkyl or $-\text{C}(\text{O})\text{R}_3$; R6 is hydrogen, lower alkyl or phenyl; X is $-\text{C}(\text{O})\text{N}(\text{R}_6)-$, $-\text{N}(\text{R}_6)\text{C}(\text{O})-$, $-(\text{CH}_2)_m\text{O}-$ or $-\text{O}(\text{CH}_2)_m-$; n is 0, 1, 2, 3 or 4 and; m is 1, 2, or 3; and to their pharmaceutically acceptable acid addn. salts. These compds. may be used as prodrugs for the treatment or prevention of illnesses, related to the NK1 receptor. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-[6-(4-oxymorpholin-4-yl)-4-o-tolylpyridin-3-yl]isobutyramide (II) and related compds. were prepd. in multistep procedures.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2001:396485 CAPLUS
DN 135:5533
TI Process for preparation of pyridine derivatives
IN Hilpert, Hans; Hoffmann-Emery, Fabienne; Rimmner, Goesta; Rogers-Evans, Mark; Stahr, Helmut Werner; Waldmeier, Pius
PA F. Hoffmann-La Roche A.-G., Switz.
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1103546	A1	20010530	EP 2000-125665	20001123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1999-123686 A 19991129				

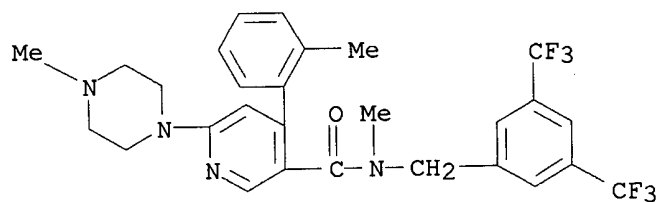
US 6303790	B1	20011016	US 2000-716538	20001120
			EP 1999-123686 A	19991129
JP 2001151755	A2	20010605	JP 2000-360682	20001128
JP 3403164	B2	20030506		
			EP 1999-123686 A	19991129
CN 1297887	A	20010606	CN 2000-128383	20001128
			EP 1999-123686 A	19991129

OS CASREACT 135:5533; MARPAT 135:5533

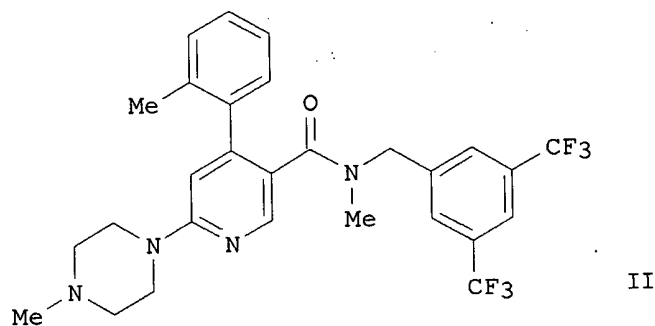
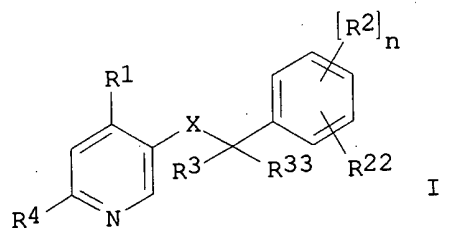
IT **290297-57-3P**RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
(Preparation)

(process for prepn. of pyridine derivs.)

RN 290297-57-3 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-
4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

GI



AB The title compds. [I; R1 = alkyl, (un)substituted aryl; R2, R22 = H, halo,

CN 1270959	A	20001025	CN 2000-102401	20000223
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
ES 2171109	A1	20020816	ES 2000-418	20000223
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
JP 2000247957	A2	20000912	JP 2000-47003	20000224
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
BG 104187	A	20001130	BG 2000-104187	20000224
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
US 2002091265	A1	20020711	US 2001-901982	20010710
US 6479483	B2	20021112		
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
			US 2000-507456 A	320000222

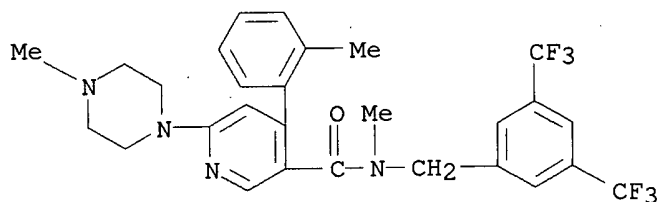
OS MARPAT 133:207811

IT 290296-52-5P 290296-83-2P 290296-84-3P
 290296-85-4P 290296-86-5P 290296-89-8P
 290296-93-4P 290296-94-5P 290296-95-6P
 290296-96-7P 290296-98-9P 290296-99-0P
 290297-00-6P 290297-11-9P 290297-12-0P
 290297-57-3P 290297-60-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of N-benzyl-4-tolylnicotinamides and related compds. as neurokinin-1 receptor antagonists)

RN 290296-52-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 290296-83-2 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

CF3, etc.; R2 and R22 may be together = (un)substituted CH:CHCH:CH; R3, R33 = H, alkyl, or forming a cycloalkyl together with the carbon atom, to which they are attached; R4 = H, alkyl, (un)substituted NH2, etc.; X = CONR5, NR5CO; R5 = H, alkyl, CH2Ph; n = 0-4], useful as antagonists of neurokinin 1 receptor (no data), were prepd. Thus, treating 6-chloronicotinic acid with SOCl2 and MeNH2.HCl followed by reaction of 6-chloro-N-methylnicotinamide with o-tolylmagnesium chloride and 1-methylpiperazine, treatment of 6-(4-methylpiperazin-1-yl)-4-o-tolyl-4,5-dihydropyridine-3-carboxylic acid methylamide with MnO2, and reacting N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide with 3,5-bis(trifluoromethyl)benzyl bromide afforded the nicotinamide II.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2000:607348 CAPLUS

DN 133:207811

TI Preparation of N-benzyl-4-tolylnicotinamides and related compounds as neurokinin-1 receptor antagonists.

IN Boes, Michael; Branca, Quirico; Galley, Guido; Godel, Thierry; Hoffmann, Torsten; Hunkeler, Walter; Schnider, Patrick; Stadler, Heinz

PA F. Hoffmann-La Roche Ag, Switz.

SO Ger. Offen., 38 pp.

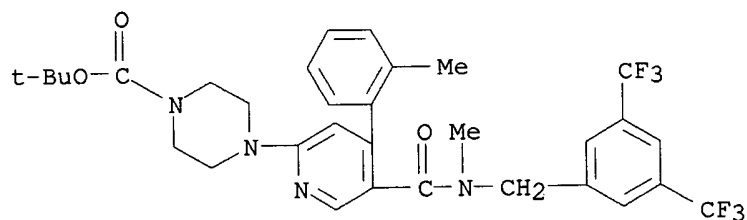
CODEN: GWXXBX

DT Patent

LA German

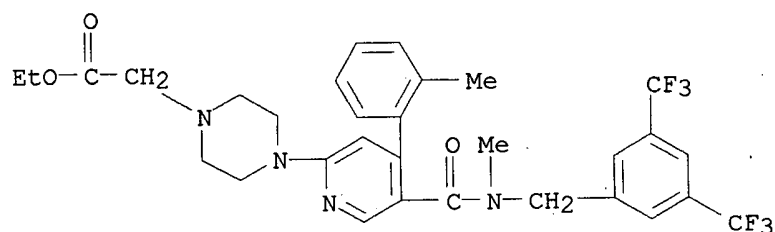
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10008042	A1	20000831	DE 2000-10008042	20000222
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
EP 1035115	A1	20000913	EP 2000-102260	20000215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
GB 2347422	A1	20000906	GB 2000-3908	20000218
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
NZ 502948	A	20010928	NZ 2000-502948	20000218
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
FR 2790473	A1	20000908	FR 2000-2170	20000222
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
US 6297375	B1	20011002	US 2000-507456	20000222
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
ZA 2000000894	A	20000824	ZA 2000-894	20000223
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NO 2000000885	A	20000825	NO 2000-885	20000223
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
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			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129



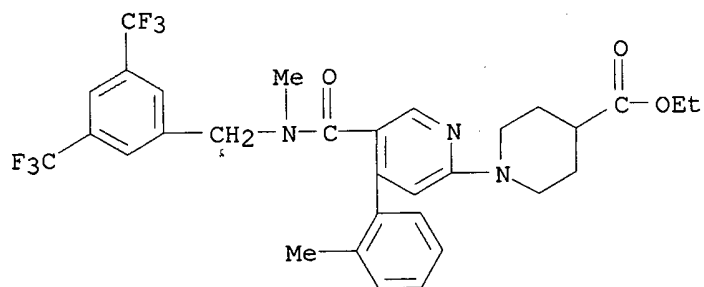
RN 290296-84-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI)
(CA INDEX NAME)



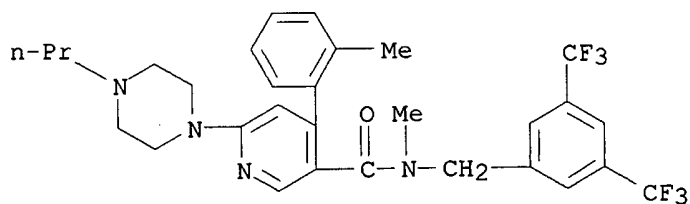
RN 290296-85-4 CAPLUS

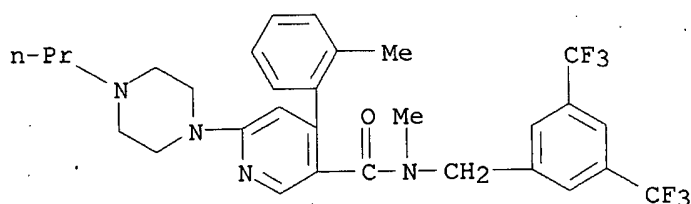
CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290296-86-5 CAPLUS

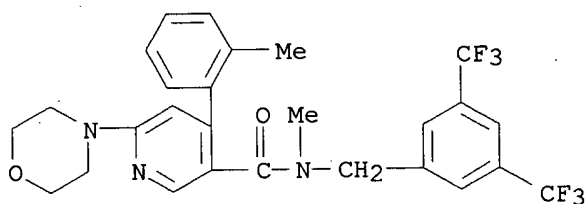
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-propyl-1-piperazinyl)- (9CI) (CA INDEX NAME)





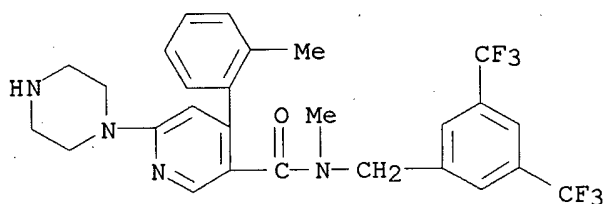
RN 290296-89-8 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



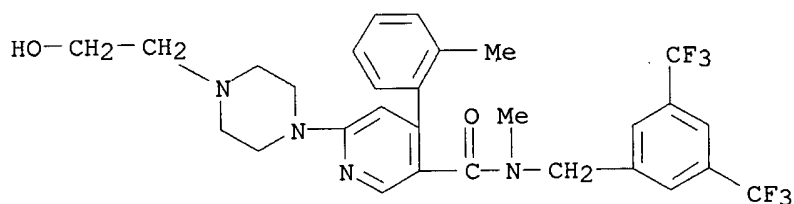
RN 290296-93-4 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



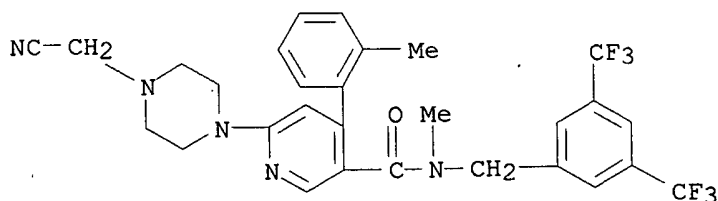
RN 290296-94-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



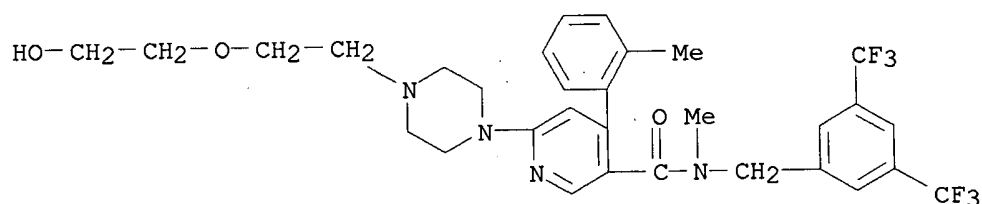
RN 290296-95-6 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(cyanomethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



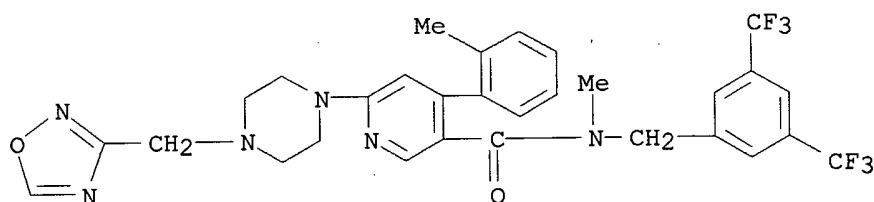
RN 290296-96-7 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI)
(CA INDEX NAME)



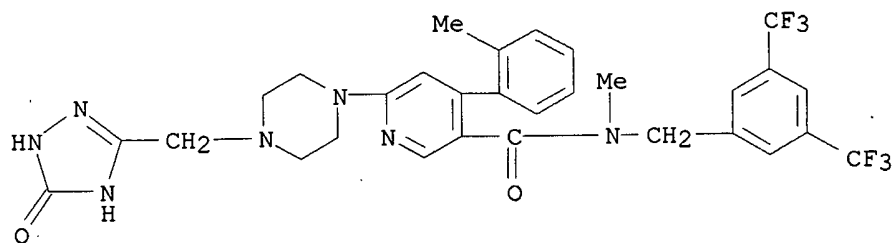
RN 290296-98-9 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-[4-(1,2,4-oxadiazol-3-ylmethyl)-1-piperazinyl]- (9CI)
(CA INDEX NAME)



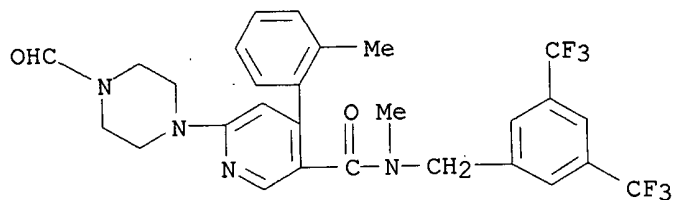
RN 290296-99-0 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)methyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

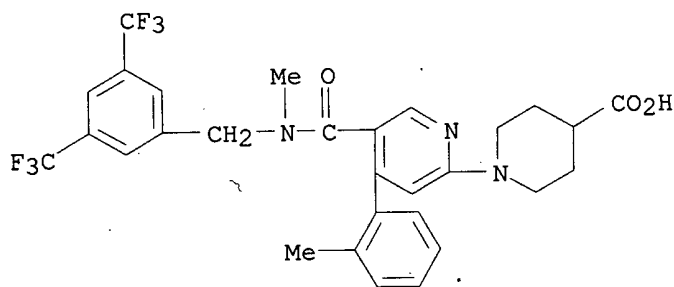


RN 290297-00-6 CAPLUS

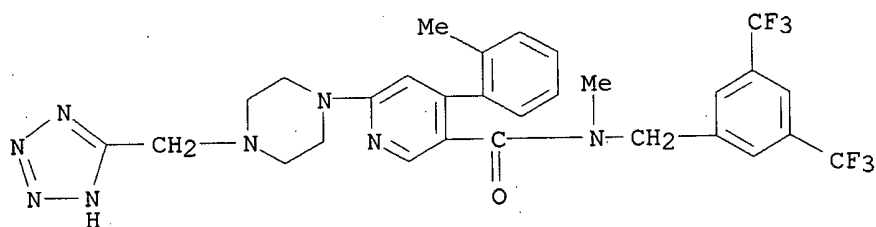
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



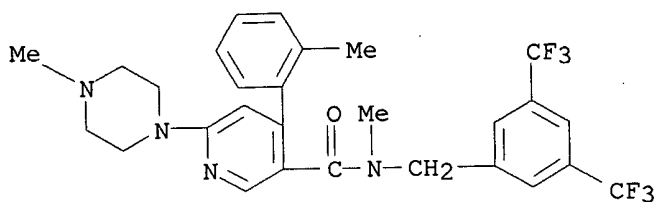
RN 290297-11-9 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 290297-12-0 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-[4-(1H-tetrazol-5-ylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

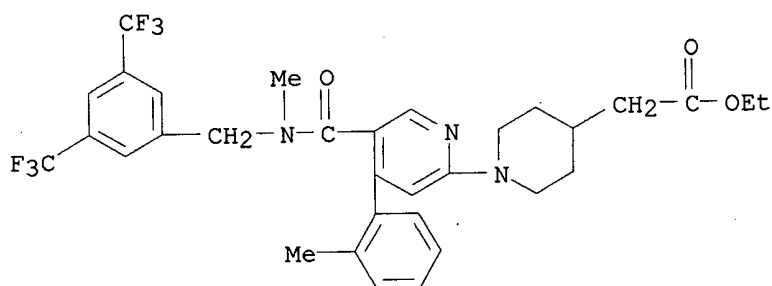


RN 290297-57-3 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

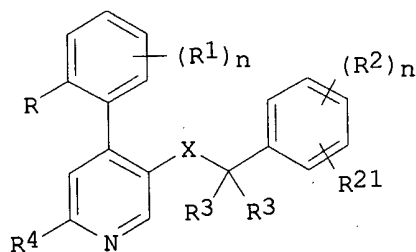


RN 290297-60-8 .CAPLUS

CN 4-Piperidineacetic acid, 1-[5-[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI)
(CA INDEX NAME)



GI



I

AB Title compds. [I; R = H, alkyl, alkoxy, halo, CF₃; R₁ = H, halo; RR₁ = CH:CHCH:CH; R₂, R₂₁ = H, halo, CF₃, alkoxy, cyano; R₂R₂₁ = (substituted) CH:CHCH:CH; R₃ = H, alkyl, cycloalkyl; R₄ = H, N(R₅)₂, N(R₅)(CH₂)nOH, N(R₅)S(O)₂A, N(R₅)S(O)₂Ph, N:CHN(R₅)₂, N(R₅)C(O)R₅, specified cyclic tertiary amine; R₅ = H, cycloalkyl, benzyl, alkyl; X = C(O)N(R₅), (CH₂)mO, (CH₂)mN(R₅), N(R₅)C(O), N(R₅)(CH₂)m; n = 0-4; m = 1, 2], were prepd. Thus, 4-o-tolylnicotinic acid (prepn. given) was stirred with SOCl₂ and cat. DMF in CH₂Cl₂ to give a residue which was refluxed with N-[3,5-bis(trifluoromethyl)benzyl]-N-methylamine and Et₃N in PhMe to give 67% N-(3,5-bis(trifluoromethyl)benzyl)-N-methyl-4-o-tolylnicotinamide. Tested I antagonized NK-1 receptors with pK_i = 8.20-9.54.

=> d his

(FILE 'HOME' ENTERED AT 08:43:03 ON 24 MAY 2003)

FILE 'REGISTRY' ENTERED AT 08:43:13 ON 24 MAY 2003

L1 STRUCTURE UPLOADED
L2 6 S L1
L3 39 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 08:43:57 ON 24 MAY 2003

L4 7 S L3

=> d cost

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.68	1.17
0.12	0.24
0.00	147.75
30.24	30.24
-----	-----
31.04	179.40
1.55	1.55
-----	-----
32.59	180.95

CAPLUS FEE (5%)

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE	TOTAL
ENTRY	SESSION
-4.56	-4.56

IN FILE 'CAPLUS' AT 08:45:05 ON 24 MAY 2003